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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/754,446	SUN ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 and 35-36 are cancelled
Claims 19-34 are pending.

This Office Action is in reply to Applicants' correspondence of 08/17/2006. Claims 1-18 and 35-36 are cancelled; no claims are withdrawn; no claims have been newly added; claims 19, 21, 22, and 25 have been amended. Applicants' remarks and amendments have been fully considered but are not found to be persuasive. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn. This Action is made FINAL.

Information Disclosure Statement

1. Applicants Remarks (p.15) concerning citation A1 (US Pat 6,028,290) on the IDS of 06/282004 indicate that the correct citation should be US Pat 6,028,190 and that a supplemental IDS for the intended reference is attached to the Remarks. The Examiner has not found a supplemental IDS with the papers filed by Applicant on 08/17/2006, thus the correct citation is included on a PTO-892 included with this Office Action.

Maintained Rejection
Claim Rejection - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 19, 23-25, 28, 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelmann et al (2002) as evidenced by GenBank AF287270 (2000) in view of Doll et al (2002).

The GenBank AF287270 sequence is the source of all nucleotide position numbers referenced in this rejection.

Edelmann et al teaches a method to screen for specific mutations (p.1023, right col., lns.14-20) responsible for causing Mucolipidosis IV. The method comprises steps of amplifying relevant portions of the MCOLN1 gene with appropriate primers (p.1024, left col., lns.26-47), and detecting the presence of wildtype or mutant gene sequences by hybridization to probes specific probes (p.1024, right col., lns.15-20).

Regarding claim 19, Edelmann et al teaches a method for determining the presence of a 6,434-bp deletion mutation spanning nucleotides 511-6,944 (designated in the reference as '511del6434') in the MCOLN1 gene. The method comprises the steps of contacting a nucleic acid sample with primers for amplification: relevant to step i) of claim 19, the MLIV-3UPS primer (p.1024, left col., lns.32-34) is complementary the 20 nucleotides from position 241 to position 260, thus satisfying the limitation of the claim that the primer is complementary to a 15-30 bp segment of DNA between positions 100-500 of the MCOLN1 gene; relevant to step ii) of claim 19, the MLIV-4UPS primer (p.1024, left col., lns.34-35) is complementary to the 20 nucleotides from position 7017 to 7036, thus satisfying the limitation of the claim that the primer is complementary to a 15-30 bp segment of DNA between positions 6956-7356 of the MCOLN1 gene. Relevant to step iii) of claim 19, Edelmann et al teaches the detection of the mutant

sequence using a probe (p.1024, right col., lns.19-20) complementary to nucleotides from positions 503-510 and positions 6944-6954, thus satisfying the limitations of the claim because the probe is complementary to a sequence that is amplified from a template DNA that possesses the 511del6434 using the primers of steps i) and ii).

Regarding claim 25, Edelmann et al teaches the multiplexing of PCR amplification for detecting the presence of one or both of the IVS3-2A→G mutation (p. 1023, right col. lns.14-16) and the 511del6434 mutation (p.1024, left col., lns.12-15; p.1024, left col., ln.47 – p.1024, right col., ln.2; Fig.1; Fig.2). The method comprises the steps of contacting a nucleic acid sample with primers for amplification, and probes for the detection of mutant sequences. Relevant to step i) of claim 25, the MLIV-1UPS primer (p.1024, left col., lns.28-29) is complementary to the 20 nucleotides from position 5361 to position 5380, thus satisfying the requirement that the primer is complementary to a 15-30 bp segment of DNA between positions 5124-5524 of the MCOLN1 gene; relevant to step ii) of claim 25, the MLIV-2UPS primer (p.1024, left col., lns.29-31) is complementary to the 20 nucleotides from position 5711 to position 5730, thus satisfying the requirement that the primer is complementary to a 15-30 bp segment of DNA between positions 5541-5941 of the MCOLN1 gene. Relevant to step iii) of claim 19, Edelmann et al teaches the detection of the mutant sequence using a probe (p.1024, right col., ln.18) that is complementary to the 19 nucleotides from position 5523 to position 5541, thus satisfying the requirement that the probe is complementary to a segment of DNA that includes position 5534 of the MCOLN1 gene. Relevant to step iv) of claim 19, the MLIV-3UPS primer (p.1024, left col., lns.32-34) is complementary the

20 nucleotides from position 241 to position 260, thus satisfying the limitation of the claim that the primer is complementary to a 15-30 bp segment of DNA between positions 100-500 of the MCOLN1 gene; relevant to step v) of claim 19, the MLIV-4UPS primer (p.1024, left col., lns.34-35) is complementary to the 20 nucleotides from position 7017 to 7036, thus satisfying the limitation of the claim that the primer is complementary to a 15-30 bp segment of DNA between positions 6956-7356 of the MCOLN1 gene. Relevant to step vi) of claim 19, Edelmann et al teaches the detection of the mutant sequence using a probe (p.1024, right col., lns.19-20) complementary to nucleotides from positions 503-510 and positions 6944-6954, thus satisfying the limitations of the claim because the probe is complementary to a sequence that is amplified from a template DNA that possesses the 511del6434 using the primers of steps iv) and v).

Regarding claim 28, Edelmann et al teaches the sequence of the mutant IVS3-2A→G probe (p.1024, right col., ln.18), which is complementary to nucleotide positions 5523-5541of the MCOLN1 gene, thus overlaps and contains the sequence of SEQ ID NO: 6 (which is complementary to nucleotide positions 5526-5540 of the MCOLN1 gene), and thus is comprised of and consists essentially of the claimed sequence.

Regarding claim 34, Edelmann et al teaches the sequence of the 'normal' IVS3-2A→G probe (p.1024, right col., ln.17), which is complementary to nucleotide positions 5523-5541of the MCOLN1 gene, thus overlaps and contains the sequence of SEQ ID NO: 5 (which is complementary to nucleotide positions 5526-5540 of the MCOLN1 gene), and thus is comprised of and consists essentially of the claimed sequence.

Edelmann et al does not teach the detection of specific sequences (the deletion mutation, the single nucleotide mutation, or the wildtype 'normal' sequence) using probes that are labeled with detectable labels (comprising a donor fluorophore and a quencher moiety), and monitoring the accumulation of amplified nucleic acid in real time by detecting changes in fluorescence.

Doll et al teaches a method to genotype several polymorphic sites within a gene using TaqMan real time PCR analysis and probes labeled with fluorescent reporters.

Relevant to claim 19 (step iii) and part b)), claim 24, claim 25 (steps iii) and vi), and part b)), and claim 33, Doll et al teaches the detection of specific sequences using a real time PCR method in which the fluorescence signal increases when the probe with the exact sequence match binds to the template DNA and is digested by the exonuclease activity of the polymerase, thus releasing the reporter dye from the quencher (p.330, right col., ln.24 – p.331, right col., ln.6; Fig.2).

Relevant to claims 23 and 32, Doll et al specifically teaches the use of the reporter dyes FAM, VIC, and TET (p.330, left col., lns.50-56).

Relevant to claim 34, Doll et al teaches the multiplexed use of the fluorescently labeled reporter probes (p.330, right col., lns.11-24; Table 2; Fig 1) for the detection of different sequences within the same nucleic acid sample.

It would have been prima facie obvious to one of skill in the art at the time the invention was made to have modified the mutation detection methods of Edlemann et al to have used the real time PCR detection methods of Doll et al et al. One would have been motivated to do so based on the assertion by Doll et al that the real time PCR

based method is a rapid method for the analysis of nucleic acid sequences that is reliable, does not require radioactivity, and is suitable for automated applications (p.331, left col., ln.7 – p.331, right col., ln.11). One would have had a reasonable expectation of success because Doll et al teaches the successful analysis of multiple nucleic acid mutations within a given nucleic acid sample (Fig.2 of Doll et al et al) similar to the analysis of the multiple mutations of the MCOLN1 gene (Fig.2 of Edelmann et al).

Response to Remarks

Applicants have traversed the rejection of claims as unpatentable over Edelmann et al as evidenced by GenBank AF287270 in view of Doll et al.

Applicants argue that not all primer pairs and probes that might wok acceptably in standard PCR as taught by Edelmann will necessarily work for real time PCR because of the more stringent requirements of real time PCR. Applicants have provided a declaration (Sun Declaration ¶ 5 and 6) asserting the opinion that primers and probes that work in standard PCR may not work in the TaqMan format, and that primers and probes in the TaqMan assay must work together in homogeneous conditions. The arguments and declaration have been fully considered but are not found to be persuasive. The arguments and declaration are not commensurate in scope with the claims; while the arguments and declaration indicate that primers and probes for a TaqMan assay must be particularly selected, the claims do not require either primers or probes consisting of a particular sequence. For example, claim 19 (drawn to a method for detecting a deletion) requires only primers comprising a sequence complementary to

any 15-30 bp region of two 400bp regions (positions 100-500 and 6956-7356) for amplification, and a probe comprising a sequence complementary to any 13-30 bp segment amplified using the two primers, and do not require any particular sequence elements. And while, for example, claim 28 limits one of the probes to comprising a sequence that consists essentially of SEQ ID NO: 6, the open nature of the terms 'comprising' and 'consists essentially of' increases the breadth of the probes encompassed by the claim beyond any one primer consisting of a discrete nucleic acid sequence. And while applicant argues that the GenBank sequence does not cure the deficiencies of Edelmann and/or Doll, the Examiner maintains that Edelmann as evidenced by the GenBank sequence teaches the entire MCOLN1 gene sequence relied upon for the claims as well as the precise molecular nature of mutations within the sequence and their detection using nucleic acid amplification and hybridization based techniques.

Applicants additionally argue that the real-time methods of Doll do not specifically teach the analysis of a large deletion mutation, and thus does not address how to use the method in the analysis of the MCOLN1 gene mutations of Edelmann. This argument has been considered but is not found to be persuasive. The teachings of Doll clearly indicate the use of real-time PCR techniques in the detection of particular sequences. While Doll does not specifically address a deletion mutations, Edelmann teaches the particular sequence that results from the deletion mutation, which is a sequence that can be detected using probe hybridization, as taught by both Edelmann and Doll.

Applicants additionally argue (p.18) that the third probe of Edelmann can only be used for the exact deletion mutation of nts 511 to 6943 because the probe binds directly to nts 504-510 linked to 6944-6954. This is not found to be persuasive because the rejected claims do not require any probe capable of detecting any particular deletion other than that disclosed by Edelmann, nor does the specification of the instant application teach any particular deletion mutation other than the deletion mutation disclosed by Edelmann. Additionally, in view of the teachings of Edelmann as evidenced by the GenBank sequence, one of ordinary skill in the art would be able multiple different probes for the detecting the presence or absence of any deleted sequence.

Applicants argue that neither Doll nor the GenBank sequence teach or suggest a way to address the difficulties of adapting MCOLN1 genotyping to real time PCR. This argument is not found to be persuasive. As is noted above, the claims to not require any probes of primers consisting of discrete nucleic acid sequences. Additionally, while the provided declaration asserts that primer and probes that work in standard PCR might not work in the TaqMan format. However the Declaration does not provide any specific evidence that the particular primers and probes of Edlemann, or any other primers or probes used in 'standard' PCR and hybridization analysis of the MCOLN1 sequence, would in fact not work in a TaqMan format. Additionally, given the sequence of the MCOLN1 gene and the particular nature of the mutations of interest, one of ordinary skill in the art would know how to generate additional primers and probes for a TaqMan-based analysis of the gene.

Applicants have argued (p.19) that claims 25, 28, and 32-34 require the real-time PCR analysis of two types of mutations in a single reaction using two primer pairs and three probes to distinguish the different amplicons. The Examiner points out that claim 25 is in fact drawn to a method of detecting the presence of 'one or two' mutations, and that the method indicates the presence of 'one or both' of the mutations.

Applicants have argued that Edelmann does not disclose the using real time PCR, and the Examiner's use of Doll et al to fill this gap is not effective because Doll teaches genotyping using real time PCR of an unrelated gene and does not teach the simultaneous detection of a single base mutation and a deletion mutation as applicant asserts is required by the claims. This argument has been considered but is not found to be persuasive. The Examiner maintains that Edelmann does in fact teach the multiplexed amplification of the MCOLN1 gene using primers for both the single base mutation and the deletion mutation (Edelmann p.1024, left col., ln. 23), and Applicant has provided no evidence that such a multiplex amplification in a TaqMan format would not have worked using these same primers, or primers designed using the GenBank sequence by one of ordinary skill in the art. While Edelmann does not teach a muliplex probe hybridization assay (with the simultaneous hybridization of different probes), Doll teaches using a TaqMan assay with three probes for the detection of three different particular nucleic acid sequences. While Doll does not teach the detection of a deletion *per se*, Edelmann teaches that the detection of the MCOLN1 deletion can be accomplished by the detection of hybridization of a probe to a particular nucleic acid

sequence generated by the deletion. Further, though Applicant asserts there are differences in the detection of particular sequences as taught by Edelmann, the detection of particular sequences taught by Doll, and the detection requirements of the claims, Applicant has provided no evidence that the detection of particular sequences using the three probes of Edelmann (i.e. the A/G normal, A/G mutant, and deletion probes), or probes designed using the GenBank sequence by one of ordinary skill in the art, would not work in a real-time PCR based method using multiple differently labeled probes for the detection of particular sequences as taught by Doll.

The Examiner maintains that Edelmann in view of the GenBank sequence teaches PCR amplification and probe hybridization based methods for the detection of particular mutations in the MCOLN1 gene using three probes to detect three particular nucleic acid sequences, and Doll teaches the use of probes labeled with three different fluorophores for the detection of particular nucleic acid sequences in a real-time PCR based assay.

The rejection is maintained.

Maintained Rejection
Claim Rejection - 35 USC § 103

4. Claims 20-22, 26, 27, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelmann et al (2002) in view of Doll et al (2002), and further in view of GenBank AFAF287270 (2000) and Buck et al (1999).

The teachings of Edelmann et al in view of Doll et al are applied to claims 20-22, 26, 27, and 29-31 as they were previously applied to claims 19, 23-25, 28, 32-34.

Edelmann et al teaches methods for detecting mutations in the MCOLN1 gene using primers and probes that are functionally equivalent (i.e. primers that amplify the relevant mutation-containing portions of the MCOLN1 gene, and probes that detect the particular mutations within the MCOLN1 gene) to the primers and probes required by the claims. Specifically, Edelmann et al teaches: the MLIV-3UPS primer (p.1024, left col., lns.32-34) which has a binding site 180nt upstream of SEQ ID NO: 3 (which hybridizes to nucleotides 441-460) ; the MLIV-4UPS primer (p.1024, left col., lns.34-35), which overlaps the 20 of the 21 nucleotides in the sequence of SEQ ID NO: 4 (which hybridizes to nucleotides 7037-7017); the 511del6434 probe (p.1024, right col., lns.19-20) for detection of the sequence created by the MCOLN1 deletion mutation which has a binding site 24nt upstream of SEQ ID NO: 7 (which hybridizes to nucleotides 6982-6997); the MLIV-1UPS primer (p.1024, left col., lns.28-29) which has a binding site 50nt upstream of SEQ ID NO: 1 (which hybridizes to nucleotides 5495-5509); and the MLIV-2UPS primer (p.1024, left col., lns.29-31) which has a binding site 10nt downstream of SEQ ID NO: 2 (which hybridizes to nucleotides 5698-5677).

Edelmann et al in view of Doll et al does not teach primers comprised of sequences that consist essentially of SEQ ID NO: 3 (as required by claims 20 and 29), SEQ ID NO: 4 (as required by claims 21 and 30), SEQ ID NO: 1 (as required by claim 26), or SEQ ID NO: 2 (as required by claim 27); or a probe comprised of a sequence that consists essentially SEQ ID NO: 7 (as required by claims 22 and 31).

GenBank AF287270 teaches the complete nucleic acid sequence of the MCOLN1 gene from humans, which includes the positions of the MLIV-4UPS, MLIV-

3UPS, MLIV-1UPS, and MLIV-2UPS primers and the 511del6434 probe from Edelmann et al, as well as SEQ ID NOs 1, 2, 3, 4 (paragraphs [0035]-[0036]; Table 1) and SEQ ID NO: 7 (paragraph [0050]; Table 2) from the instant application. Furthermore, Buck et al expressly provides evidence of the equivalence of primers. Specifically, Buck et al invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck et al also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18mer primers on the 300 base pair sequence (see page 530, column 1). When Buck et al tested each of the primers selected by the methods of the different labs, Buck et al found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck et al expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck et al provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Therefore, it would have been prima facie obvious to one of skill in the art at the time the invention was made to have modified the detection methods of Edelmann et al

in view of Doll et al to use any primers based on the MCOLN1 gene sequence of GenBank AF287270, especially sequences which are in close proximity to those taught by Edelman et al. One would have been motivated to use any appropriate primers within the MCOLN1 sequence based on the assertion of Edelmann et al that MCOLN1 gene mutations are useful for screening for Mucolipidosis Type IV. One would have been motivated to modify the primers taught by Edelmann et al in order to have provided additional primer pairs useful in Mucolipidosis Type IV screeining. One would have had a reasonable expectation of success based on the indication of Edelmann et al that amplification and probing methods can be used to detect Mucolipidosis Type IV related mutations in the MCOLN1 gene, and the results of Buck et al that teach the successful use of primers with a wide variety of sequences.

Response to Remarks

Applicant has traverse the rejection arguing that the disclosure of Buck merely describes sequencing primers which are unrelated to the present invention. The argument has been considered but is not found to be persuasive. The Examiner maintains that while Buck does teach primers of an unrelated sequence, the important teaching of Buck lies in the general teaching of the equivalence of different primers. Thus given the disclosed MCOLN1 sequence and the particular nature of the mutations and their detection via primer amplification/probe hybridization techniques, one of ordinary skill in the art would be able to design primers which satisfy the limitations of

the claims for use in an assay as taught by Doll et al which is an amplification/hybridization based assay.

Applicant particularly takes issue (p.20) with the Examiners assertion that any primer or probe in a given sequence would be equivalent. Applicant provides that Bernard et al (1998) teaches that genotyping with multiplexed hybridization probes has technical challenges and limitations in addition to the optimization often necessary for multiplexing primer sets, and also provides in the Declaration that asserts that primers for standard PCR may not work in TaqMan format. The arguments have been considered but are not found to be persuasive. Initially it is noted that Bernard teaches a multiplexed assay based on the different melting temperatures of multiple hybridized probes, and not the nuclease based TaqMan method of the instant claims and art applied by the Examiner. Applicant has provided no evidence of any particular difficulty in the design of successful primers and probes for the multiplex analysis of the MCOLN1 gene mutations. Additionally, the teachings of Edelmann indicate that the primers used for amplification of the MCOLN1 gene can be used in a multiplex format, and that the different particular probes can be hybridized under the same conditions as each other (p.1024, right col., last paragraph), indicating that they may be suitable for simultaneous use in a multiplex assay. Furthermore, the teachings of Bernard et al and Section 5.1 in Real-Time PCR (Declaration ¶ 7) indicate that optimization of primers and probes in a TaqMan format would be standard experimentation expected of one of skill in the art. Finally, as indicated in the earlier Response to Remarks, the asserted requirement of particular probes and primers for use in a multiplexed assay is not

commensurate in scope with the recited limitations of the claims. For example, claim 20 limits one of the primes to an oligonucleotide comprising a sequence that consists essentially of SEQ ID NO: 3,where the open nature of the terms 'comprising' and 'consists essentially of' increases the breadth of the primers encompassed by the claim beyond any one primer consisting of a discrete nucleic acid sequence.

The rejection is maintained.

Response to the Declaration

As addressed in the previous Response to Remarks, the declaration supplied by applicant has been fully considered but is not found to be persuasive to overcome the rejections. The Declaration provides no specific evidence or the results of any particular experimentation indicating any unexpected results regarding design of primers and probes for the multiplexed analysis of the MCOLN1 gene. Furthermore, the Declaration does not provide that the design of primers and probes for the successful analysis of the MCOLN1 gene would require any experimentation beyond that required for the development of a typical assay (or beyond the teaching of the references applied by the Examiner) or beyond the capabilities of one of ordinary skill in the art. Additionally, while the Declaration asserts that only particular primers and probes are suitable for a multiplexed assay, the claims encompass primers and probes well beyond this assertion. Thus, for example, while the specification teaches the results of a multiplex assay using particular primers (Table 1) and probes (Table 2), the claims encompass assays using primers and probes of a wide variety of sequences.

Conclusion

No claim is free of the prior art. No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Kapushoc
Art Unit 1634

CARLA J. MYERS
PRIMARY EXAMINER